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September 12, 2000

SELECTED KEY STUDIES ON PARTICULATE MATTER AND HEALTH: 1997 - 2000

NEW STUDIES CONFIRM THAT CURRENT LEVELS OF PARTICULATE AIR POLLUTION ARE HARMFUL TO HUMAN HEALTH

The Clean Air Act requires the U.S. Environmental Protection Agency (EPA) to review and update the National Ambient Air Quality Standards for major air pollutants every five years, in light of the latest scientific evidence.

More than 500 new scientific studies examining the effect of airborne particulates on human health have been published since 1996, when EPA last reviewed the particulate standards. The new studies validate the earlier research and address many of the arguments raised by industry critics. Taken together, the studies confirm the relationship between particulate air pollution, illness, hospitalization, and premature death.

New analyses show that lives may be shortened by months or years, rather than days.
Recent studies of laboratory animals and humans have identified cardiac responses to particles, thus elucidating possible biologic mechanisms for mortality.
New studies demonstrate that infants and children are especially sensitive to the effects of fine particle pollution.

In 1997 when EPA announced the establishment of new NAAQS for fine particles, the President directed EPA to complete a review of the standards by July 2002.

The National Academy of Sciences (NAS) has issued several reports recommending research priorities to increase scientific understanding of particle pollution. To address the scientific issues raised by the NAS panel, EPA increased funding for research on particulates to more than $50 million per year. As part of this effort, the Health Effects Institute, jointly sponsored by industry and EPA, has committed substantial resources to research on PM.

As a result of this infusion of research funds, hundreds of scientific papers and research reports have been published since EPA last issued its "Air Quality Criteria for Particulate Matter" in 1996.

This annotated bibliography presents the findings of some of the most significant new research studies that advance our understanding of the harmful health effects of particulate air pollution. The peer-reviewed papers cited here represent a small sample of the scientific articles on the health effects of particulate air pollution published since 1996. This bibliography does not attempt to be comprehensive: exclusion does not imply that a study is unimportant; inclusion does not imply endorsement.

LONG-TERM STUDIES OF MORTALITY

Prospective Cohort Epidemiological Studies Are Validated in Independent Reanalysis

Two landmark prospective cohort studies reported that chronic exposure to particulate pollution increases the risk of premature mortality. In the 1993 Six Cities Study, Harvard University researchers followed the health of more than 8,000 people in six small cities that fell along a gradient of air pollution concentrations for a period of 14 to 16 years. As particle concentrations increased, there was an almost directly proportional increase in the death rate in the residents studied. Residents of the most polluted city in the study, **Steubenville**, Ohio, had a 26 percent increased risk of premature mortality, compared to the residents of the cleanest city studied, **Portage**, Wisconsin. The increased risks were associated with a difference in ambient fine particle concentrations of 18.6 micrograms per cubic meter.

The 1995 American Cancer Society study reported an association between fine particle air pollution and premature death by cardio-pulmonary and other causes in a study group of over half a million people in **151 U.S. cities**. All cause mortality increased by 17 percent with a 24.5 microgram per cubic meter difference in fine particle pollution between the cleanest and dirtiest city studied.

These original studies used statistical techniques to adjust for age, and to control for the effects of smoking, diet, and occupational exposure.

Health Effects Institute funded researchers, led by Dr. Dan Krewski of the University of Ottawa, undertook a reanalysis of the original studies and a quality audit of the underlying data. Researchers performed an extensive sensitivity analysis using alternative statistical methods, and considering the role of 20 potential confounders such as other pollutants, climate, and socio-economic factors on study results. The sensitivity analysis largely confirmed the original results of the Harvard Six Cities Study and the American Cancer Society Study. In addition, the sensitivity analysis identified higher educational status as a factor associated with reduced risk to air pollution exposure, and reported an association between sulfur dioxide pollution and mortality.

Krewski, D., Burnett, R.R., Goldberg, M.S., Hoover, K., Siemiatycki, J., Jerrett, M., Abrahamowicz, M., White, W.H, and Others. Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. Health Effects Institute, July, 2000.

Dockery, D.W., Pope, C.A., Xu, X., Spengler, J.D., Ware, J.H., Fay, M.E., Ferris, B.G., and Speizer, F.E. An Association Between Air Pollution and Mortality in Six U.S. Cities. New England Journal of Medicine, 1993:329:1753-9.

Pope, C.A., Thun, M.J., Namboodiri, M.M., Dockery, D.W., Evans, J.S., Speizer, F.E., and Heath, C.W. Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults. American Journal of Respiratory Critical Care Medicine, 1995:151:669-7

Chronic Exposure to Particulate Pollution Shortens Lives by One to Three Years

There have been two recent attempts to quantify the extent of life shortening predicted by the long-term epidemiological studies. Dutch scientist Dr. Burt Brunekreef made such an estimate in a paper prepared for the World Health Organization's consideration of revisions to the Air Quality Guidelines for Europe. Using risk ratios reported in the Harvard Six Cities Study and the Study of the American Cancer Society cohort, Brunekreef conducted a life table analysis to estimate the effect of particulate air pollution on the survival rate of 25 year-old Dutch men. An extrapolation based on U.S. life tables yields an estimated diminished life expectancy of 1.31 years due to ambient pollution.

Dr. C. Arden Pope III, of Brigham Young University, analyzed reductions in life expectancy in the U.S. population due to chronic exposure to particulate matter. He applied relative risks for premature death derived from the prospective cohort studies, and estimated loss of life expectancy ranging from one to three years, depending upon assumptions about the age at which susceptibility to the effects of air pollution begins.

Brunekreef, Burt. Air Pollution and Life Expectancy: Is There a Relation? Occup Environ Med 1997 Nov; 54(11):781-4.

Pope, C.A. III, Epidemiology of Fine Particulate Air Pollution and Human Health: Biological Mechanisms and Who's at Risk? Envir Health Persect 108 (suppl 4):713-723 (2000).

DAILY MORTALITY STUDIES

90-City National Morbidity, Mortality and Air Pollution Study (NMMAPS) Demonstrates Effects at Current U.S. Concentrations

The Health Effects Institute, which is jointly funded by EPA and industry, commissioned an original nationwide study of the short-term effects of air pollution on human health, known as the National Morbidity, Mortality and Air Pollution Study, or NMMAPS. A team of investigators led by Dr. Jonathan Samet of the Johns Hopkins University School of Public Health developed and applied a standardized methodology for examining pollution effects across many cities. Investigators from Johns Hopkins University and Harvard University developed and applied state-of-the-art statistical techniques to examine the effects of multiple pollutants, the extent of life-shortening, and the degree of "exposure measurement error" due to reliance on centrally located air quality monitors.

In its study of the **90 largest U.S. cities**, NMMAPS found strong evidence linking daily increases in particulate pollution to increases in death. On average, overall mortality increased by 0.5 percent for every 10 microgram per cubic meter increase in PM_{10} measured the day before death. The effect was slightly greater for deaths due to heart and lung disease than for total deaths. This risk ratio is somewhat lower than reported by earlier meta-analyses, perhaps due to certain methodological assumptions such as a one- day lag.

Samet et al. report that the relative increases in daily mortality partly reflect life shortening on the order of months. The association between particulate matter and mortality persists even when other pollutants are

included in the statistical model. Their analyses also provide evidence against arguments that exposure measurement error could explain the associations between particulate matter and adverse health effects.

In addition, in a study of 14 U.S. cities, NMMAPS found strong and consistent associations between particulate air pollution and hospital admissions among the elderly. Hospital admissions data was obtained from the Medicare program. The cities were selected for study because they had daily PM_{10} measurements.

For each 10 microgram per cubic meter increase in PM_{10}, there was approximately a 1 percent increase in hospital admissions for cardiovascular disease, and about a 2 percent increase in admissions for pneumonia and chronic obstructive pulmonary disease. Cities studied were **Birmingham, AL, Boulder, CO, Canton, OH, Chicago, IL, Colorado Springs, CO, Detroit, MI, Minneapolis/St. Paul, MN, Nashville, TN, New Haven, CT, Pittsburgh, PA, Provo/Orem, UT, Seattle, WA, Spokane, WA, and Youngstown, OH**.

Investigators concluded that the complementary analyses of mortality and morbidity provide "*new and strong evidence*" linking particulate air pollution at current levels to adverse health effects.

Samet, J.M., Dominici, F., Zeger,S.L., Schwartz, J., and Dockery, D.W. The National Morbidity, Mortality, and Air Pollution Study. P
I: Methods and Methodologic Issues. Health Effects Institute Research Report 94, Part I, May 2000.

Samet, J.M., Zeger, S.L., Dominici, F., Curriero, F., Coursac, I., Dockery, D.W., Schwartz, J., and Zanobetti, A. The National Morbidi
Mortality, and Air Pollution Study. Part II: Morbidity, Mortality and Air Pollution in the United States. Health Effects Institute Rese
Report 94, Part II, June 2000.

Air Pollution Effects Persist for Several Days, Increasing the Overall Risk of Exposure

Epidemiological studies have used different assumptions about the number of days following exposure to air pollution that effects will occur. Some studies have assumed that effects occur the day after exposures. However, toxicological evidence suggests that effects of exposure may be observed over several subsequent days. In an analysis using data from **New Haven, Birmingham, Pittsburgh, Canton, Detroit, Chicago, Minneapolis, Colorado Springs, Spokane, and Seattle**, Dr. Joel Schwartz, of the Harvard School of Public Health, has shown that statistical models that assume a one day lag grossly underestimate the effect of PM_{10} on mortality. Assuming that effects continue over several days, as demonstrated by this analysis, roughly doubles the relative risk of premature mortality.

Schwartz, Joel. The Distributed Lag Between Air Pollution and Daily Deaths. Epidemiology 2000;11:320-326).

Daily Mortality Studies Pour In From Cities Around the World

Studies in new locations and by additional investigators with consistent results help strengthen the case for a causal relationship.

EPA's 1996 review of the PM standards cited over two dozen short-term epidemiological studies. Since then, time series studies reporting an association between short-term exposure to particulate matter and early mortality have been published for these U.S. cities: **Philadelphia**; **Ogden**, **Salt Lake City**, and **Provo/Orem**,

Utah; **Seattle**; **Santa Clara County**, **California;** and **Buffalo**. Additional studies have been published for these major cities all over the world: **Toronto; Mexico City; London; Edinburgh**; **Birmingham**, **UK**; **Rotterdam**; **Helsinki**; **Madrid**; **Rome**; **Milan; Brisbane; Sydney**; **Delhi; Bangkok;** and **Seoul** and **Ulsan**, **Korea**. Many of the new studies have evaluated the sensitivity of the estimated PM effects to the inclusion of other pollutants in the statistical model. Overall, the associations of PM with adverse effects continue to be consistently observed, and sometimes, effects of other air pollutants such as ozone, sulfur dioxide, nitrogen dioxide, and carbon monoxide are also reported.

A multi-city study of the short-term health effects of air pollution on mortality and hospital emergency admissions was initiated by the European Union Environment Programme. The study, known as Air Pollution and Health: A European Approach or APHEA, investigated the effects of several pollutants on mortality in 12 European cities.
The study reported positive associations with sulfur dioxide and PM_{10}, and daily increases in mortality, with stronger and more consistent associations observed in western European cities.

A quantitative meta-analysis by Jonathan Levy et al. of the Harvard School of Public Health set out to compare mortality estimates from over twenty daily time series studies. Their analysis estimated that mortality rates increased by approximately 0.7 percent per 10 microgram per cubic meter increase in PM_{10} concentrations. Investigators reported "*our model finds compelling evidence that the PM_{10}-mortality relationship is stronger in locations with higher $PM_{2.5}/PM_{10}$ ratios, supporting the hypothesized role of fine particles*."

U.S. EPA Office of Research and Development. Air Quality Criteria for Particulate Matter. EPA/600/P-99/002b, Oct. 1999, External Review Draft.

Katsouyanni, K., Touloumi, G., Spix, C., Schwartz, J., Balducci, F., Medina, S., Rossi, G., Wojtyniak, B., Sunyer, J., Bacharova, L., Schouten, J.P., Ponka, A., and Anderson, H.R. Short Term Effects of Ambient Sulphur Dioxide and Particulate Matter on Mortality i European Cities: Results From Time Series Data From the APHEA Project. British Medical Journal 1997; 314:1658 (7 June).

Levy, J. I., Hammitt, J.K., and Spengler, J.D. Estimating the Mortality Impacts of Particulate Matter: What can be Learned from Betw Study Variability? Environ Health Perspect 108:109-117(2000).

Mortality Reported in Short Term Community Health Studies is Not Due to "Harvesting"

Numerous short-term epidemiological studies have reported that short-term increases in air pollution are followed by an increased number of deaths. Some have argued that the associations between day to day variations in mortality and air pollution represent a "harvesting" effect, that is, the advancement of death by a few days in people already about to die from other causes. If air pollution advances death of the very frail by only a few days (the "harvesting" hypothesis), then you would expect that an increase in daily deaths would be followed by a decrease in deaths within a few days.

Professors Scott Zeger and Francesca Dominici of the Johns Hopkins School of Public Health developed a statistical technique to examine harvesting using data on total suspended particulate matter (TSP) and total mortality in **Philadelphia**. They found that removing the shortest term fluctuations from their time series increased rather than decreased the estimates of pollution effects. This is the opposite of what would be expected if "harvesting" accounted for all the deaths.

As part of the NMMAPS study, Dr. Joel Schwartz of the Harvard School of Public Health studied this issue using data from **Boston**. He reported that for chronic obstructive pulmonary disease and ischemic heart disease, most of the deaths seem to be advanced by a few months on average. The statistical approach did not allow estimates of life shortening beyond two months. In contrast, for pneumonia, the analysis showed that some deaths are brought forward by a few days, consistent with the harvesting hypothesis. Effect estimates increased when examining longer time periods, suggesting that cumulative exposures are more harmful than daily exposures. Overall, these results suggest that the short-term epidemiological studies underestimate the number of early deaths.

Zeger, S.L., Dominici, F, and Samet, J. Harvesting-Resistant Estimates of Air Pollution Effects on Mortality. Epidemiology 1999 Mar;10(2):171-5.

Schwartz, Joel. Harvesting and Long Term Exposure Effects in the Relation between Air Pollution and Mortality. Am J Epidemiol 20 151:440-8.

Air Quality Monitors Can Be Used to Track Exposure to Fine Particles

Epidemiological studies generally rely on centrally located air quality monitors to assess exposure to ambient air pollutants. Some have argued that these monitors do not represent actual exposures, because people spend a large portion of their day indoors.

A study by Dutch scientist Nicole Janssen et al., of 10 – 12 year old school children in **Wageningen, The Netherlands** compared personal exposure to fine particles with classroom concentrations, and with ambient measurements at an outdoor location. Researchers found that personal fine particle concentrations were highly correlated with ambient concentrations. This finding supports the use of ambient monitoring measurements as an indicator of exposure to fine particles in epidemiological time series studies.

Dr. David Mage, of U.S. EPA's Office of Research and Development, and colleagues, demonstrated that human exposure to fine particles of ambient origin is highly correlated in time to ambient PM concentrations measured at monitoring stations within the communities being studied.

The NMMAPS study discussed above also addressed the issue of measurement error, through the development of a model to systematically test what effect the relationship between personal exposure and ambient exposure might have on the observed increase in mortality associated with PM. While data to test the model is limited, "*theoretical and actual analyses generated appear to refute the criticisms that exposure measurement error could explain the associations between PM and adverse health effects.*"

Janssen, N.A.H., Hoek, G., Narssema, H., and Brunekreef, B. Personal Exposure to Fine Particles in Children Correlates Closely with Ambient Fine Particles. Archives of Environmental Health, March/April 1999, Vol. 54, No., 2, 95-101.

Mage, D., Wilson, W., Hasselblad, V., Grant, L. Assessment of Human Exposure to Ambient Particulate Matter. J. Air & Waste Ma Assoc. 49:1280-1291, Nov. 1999.

Zeger, S.L., Thomas, D., Dominici, F., Samet, J.M., Schwartz, J., Dockery, D.W., and Cohen, A. Exposure Measurement Error in Time Series Studies of Air Pollution. In: The National Morbidity, Mortality, and Air Pollution Study, Part I: Methods and Methodologic I HEI Research Report 94, May 2000.

Criteria for Asserting Causality Have Been Met

In responding to an article by Dr. John Gamble, Epidemiologist for Exxon Biomedical Sciences, Dr. David Bates, Professor Emeritus of Medicine at University of British Columbia, has re-evaluated the recent evidence health evidence regarding particulate matter and mortality. Determination of causality does not rest on any one study. Instead, a weight of evidence approach is used to evaluate the scientific literature across a series of criteria such as coherence, consistency, strength of association, temporality, analogy, and biologic plausibility. Dr. Bates asserts that all of these criteria have been met by an avalanche of new data that strengthen the case for a causal relationship.

Bates, D.V. Lines that Connect: Assessing the Causality Inference in the Case of Particulate Pollution. Environ Health Perspect 108: 2000.

Gamble, John F. $PM_{2.5}$ and Mortality in Long-term Prospective Cohort Studies: Cause-Effect or Statistical Associations? Environ Hea Perspect 106:535-549 (1998).

Kunzli, N. and Tager, I.B. Comments on "$PM_{2.5}$ and Mortality in Long-term Prospective Cohort Studies: Cause-Effect or Statistical Associations?" and Gamble, John. Reply to Kunzli and Tager Regarding Causality in PM Studies. Environ Health Perspect 107-5, 1999; Correspondence.

BIOLOGIC MECHANISMS AND CARDIAC EFFECTS

Air Pollution Tied to Low Heart Rate Variability, a Risk Factor for Heart Attacks

Particulate air pollution has been linked to cardiovascular mortality in a number of studies, but the mechanisms for this effect are not well understood. Recent research centers on the effect of pollution on heart rate and heart rate variability. Low heart rate variability is a marker of poor cardiac control by the autonomic nervous system, and is associated with a higher risk of heart attacks and sudden cardiac death. One hypothesis is that inhalation of particle air pollution may trigger an inflammatory response in the lung, followed by the release of chemical mediators that affect autonomic nervous system control of the heart beat.

Pope, et al. measured oxygen saturation and pulse rate in a panel of 90 elderly residents of the **Utah Valley**, using a small medical device known as an oximeter. The experiment was conducted during the winter months, when PM concentrations are highest. Researchers found little evidence of pollution effects on the oxygen carrying capacity of the blood, but observed that a small elevation in pulse rate was associated with a rise in PM_{10} levels. The medical and biological relevance of this effect is unclear.

Dr. Duanping Liao, of the University of North Carolina, and co-investigators, conducted daily electrocardiogram measurements on elderly nursing home residents outside **Baltimore**, Maryland. Harvard physician Dr. Diane Gold et al. studied 53- to 87- year old active residents of **Boston**. 25 minutes of electrocardiogram measurements during different exercise states were taken on a weekly basis. Both the

Baltimore and Boston studies found that elevated concentrations of fine particulate matter were associated with lower heart rate variability, and that the association was stronger for people with pre-existing cardiovascular conditions.

Pope, C.A., Dockery, D.W., Kanner, R.E., Villegas, G.M., and Schwartz, J. Oxygen Saturation, Pulse Rate, and Particulate Air Pollutio Daily Time-Series Panel Study. Am J Respir Crit Care Med 1999; 159:363-372.

Liao, D., Creason, J., Shy, C., Williams, R., Watts, R., and Zweidinger, R. Daily Variation of Particulate Air Pollution and Poor Cardiac Autonomic Control in the Elderly. Environ Health Perspect 107:521-525 (1999).

Gold, D.R., Litonjua, A., Schwartz, J., Lovett, E., Larson, A. Nearing, B., Allen, G., Verrier, M., Cherry, R., and Verrier, R. Ambient Pollution and Heart Rate Variability. Circulation. 2000;101:1267.

Stone, P.H. and Godleski J.J. First Steps Toward Understanding the Pathophysiologic Link Between Air Pollution and Cardiac Mort Am Heart J 1999;138:803-7.

Increased Heart Rate and Plasma Viscosity During an Air Pollution Episode Suggest Possible Mechanisms

The World Health Organization Monitoring Survey of Trends and Determinants in Cardiovascular Disease (the "MONICA" survey) took place in **Augsburg**, in Southern Germany during the winter of 1984-1985. Over 4,000 randomly selected adults participated, and received electrocardiograms to measure their resting heart rate, and donated blood samples to measure plasma viscosity. Electrocardiograms were administered again in 1987-1988.

In January 1985, an air pollution episode occurred throughout central Europe, with elevated concentrations of sulfur dioxide, total suspended particulates, and carbon monoxide. During the air pollution episode, higher heart rates were observed for men and women, after adjusting for cardiovascular risk factors and weather. An elevated resting heart rate is a risk factor for death and fatal heart disease, and may signal changes in the autonomic control of the heart, that might partially account for the adverse health effects observed in association with air pollution.

One hypothesis is that increased plasma viscosity might lead to constricted blood flow in the heart (ischemia), which can be fatal in people with severe coronary heart disease. During the air pollution episode, increases in plasma viscosity were observed, and persisted after adjusting for other cardiovascular risk factors and weather. German researcher Annette Peters, et al. conclude that "*the increased plasma viscosity observed in these analyses of a cross-sectional survey might therefore represent a part of the pathophysiological chain linking high ambient air pollution to increased mortality and hospital admissions for cardiovascular diseases.*"

An alternate hypothesis is proposed by Professsor Anthony Seaton of the University of Aberdeen Medical School. He collected blood samples from 112 elderly people in two cities in the U.K. over an 18-month period, and examined various blood values in comparison to PM_{10} concentrations. Based on the analysis, Seaton suggests that inhalation of some component of PM_{10} may cause sequestration of red blood cells, which may explain the cardiovascular effects reported in other studies.

Peters, A., Perz, S., Doring, A., Stieber, J., Koenig, W., and Wichmann, H.E. Increases in Heart Rate During an Air Pollution Episode Epidemiol 1999; 150:1094-8.

Peters A., Doring A., Wichmann H.E., and Koenig, W. Increased Plasma Viscosity During an Air Pollution Episode: A Link to Morta Lancet 1997 May 31; 349(9065):1582-7.

Seaton, A., Soutar A., Crawford, V., Elton, R., McNerlan, S., Cherrie, J., Watt, M., Agius, R., Stout, R. Particulate Air Pollution and th Blood. Thorax 1999 Nov;54(11):1027-32.

Heart Patients Vulnerability to Potentially Fatal Arrhythmias Increases After Exposure to Air Pollution

A pilot study was designed to test the hypothesis that heart patients with a history of serious arrhythmia requiring implanted cardiac defibrillators experience potentially life-threatening arrhythmias following short term increases in air pollution. Defibrillators monitor electrical activity of the heart and initiate interventions such as pacing or shock therapy to restore a normal heartbeat. The devices record information on arrhythmic events.

One hundred heart patients in **eastern Massachusetts** were followed for a three-year period. The study found that a subgroup of these patients -- those with more than ten defibrillator events -- were most susceptible to pollution, with effects occurring one to two days after exposure. Among these patients, the strongest associations were with nitrogen dioxide, but positive associations were reported for PM_{10} and $PM_{2.5}$ exposures as well.

Peters, A., Liu, E., Verrier, R.L., Schwartz, J., Gold, D.R., Mittleman, M., Baliff, J., Oh, J.A., Allen, G., Monahan, K., and Dockery, D.W Air Pollution and Incidence of Cardiac Arrhythmia. Epidemiology 2000 Jan; 11(1):11-7.

Combustion Source Metals May Trigger Biologic Responses to Ambient Particulate Matter

Researchers have been trying to determine whether one component of particulate matter – such as metals – is responsible for the toxic effects. U.S. EPA investigators led by Dr. Daniel Costa obtained samples of particulate matter from oil and coal fly ash and ambient air from **St. Louis, MO**, **Washington, DC**, **Dusseldorf, Germany**, and **Ottawa, Canada**. The fly ash is rich in metal components such as iron, copper, nickel, vanadium, and zinc, as well as sulfate. Laboratory rats were instilled with PM samples from these sources, and lung cells were obtained via bronchoalevolar lavage and analyzed for signs of cell injury. Investigators found that the constituent metals and their bioavailability determine the acute inflammatory response of PM samples in lung tissue.

In a second experiment, rats were pretreated with a chemical intended to model certain disease conditions, namely inflammation of blood vessels and high blood pressure in the lungs. These animals were instilled with the fly ash samples, and lung cells were obtained for laboratory examination. After 96 hours of exposure, there was clear evidence of lung inflammation, however many of the test animals had died, apparently due to altered cardiac function. Survivors had increased electrocardiographic changes. Investigators hypothesize that soluble metals from PM mediate an array of injuries to the cardiopulmonary system of healthy and at-risk subjects.

Costa, D. L., and Dreher, K.L. Bioavailable Transition Metals in Particulate Matter Mediate Cardiopulmonary Injury in Healthy and Compromised Animal Models. Environ Health Perspect 105(Suppl 5):1053-1060 (1997).

Laboratory Research on Dogs Suggests that PM May Harm People with Heart Disease

This toxicology study by Harvard pathologist Dr. John Godleski is one of the first to test whether exposure to particulate matter can change heart function in laboratory animals. Two groups of dogs were tested – healthy dogs, and dogs with an induced coronary occlusion intended to simulate human coronary artery disease. Researchers exposed dogs to concentrated particles from the ambient **Boston** air. Both the normal and the compromised animals showed effects, but the clearest sign of PM effects was found in the dogs with the induced heart condition. The occluded animals were more susceptible to serious arrhythmias when exposed to air pollution. The electrocardiogram signals for these dogs indicated more rapid development of ischemia, an inadequate flow of blood through the heart that can lead to a heart attack. Study reviewers concluded: *"this is a plausible and important mechanism to explain the association of increased cardiopulmonary mortality and exposure to particle pollution.*"

Godleski, J.J., Verrier, R.L., Koutrakis, P., and Catalano, P. Mechanisms of Morbidity and Mortality from Exposure to Ambient Air Particles. Health Effects Institute Research Report Number 91, February 2000.

Concentrated Air Particles Induce Pulmonary Inflammation and Blood Changes in Humans

Effects of particles are showing up not only in laboratory animals, but also in a chamber study with human subjects performed by EPA research physician Dr. Andrew Ghio and colleagues. This controlled exposure study of young, healthy volunteers examined the effect of exposure to concentrated ambient particles from **Chapel Hill**, North Carolina. Volunteers alternated between moderate exercise and rest over a two-hour period in a chamber with high particle concentrations. No symptoms or decrements in pulmonary function were noted. However, eighteen hours after exposure, lung tissue had a higher concentration of neutrophils, a marker of inflammation. Blood work indicated a higher concentration of fibrinogen, which is a risk factor for clotting and heart attacks.

Ghio, A.J., Kim, C., and Devlin, R.B. Concentrated Ambient Air Particles Induce Mild Pulmonary Inflammation in Healthy Human Volunteers. In Press.

HOSPITAL AND EMERGENCY ROOM VISITS

Air Pollution May Account for Five Percent of Cardiac Hospital Admissions

Numerous studies have focused on mortality because it is an easy to measure effect for which data is readily available. It is important to note that early deaths represent just the tip of the iceberg of particulate related health effects. For each death, there are many more people admitted to the hospital, and for each hospital admission, many more visits to emergency departments and doctors offices. Similarly, for each patient who visits an emergency clinic, many more experience uncomfortable respiratory symptoms or days when they must restrict their activity, increase their use of medication, or remain indoors.

Increased hospital admission rates represent one of the most serious effects of air pollution. This study examined the association between PM_{10}, carbon monoxide, and hospital admissions of the elderly for heart disease across eight urban counties with different pollution and weather profiles. The eight locations are: **Chicago**; **Colorado Springs**; **New Haven**; **Minneapolis**; **St. Paul**; **Seattle**; **Spokane**; and **Tacoma**. The study design was intended to minimize confounding by weather or other pollutants. Associations of both PM_{10} and CO with cardiovascular hospital admissions were observed in areas with widely varying correlations between these pollutants and weather factors or other air pollutants. Overall, the results suggest that air pollution may be responsible for five percent of hospital admissions for heart disease, representing an enormous public health impact.

Schwartz, Joel. Air Pollution and Hospital Admissions for Heart Disease in Eight U.S. Counties. Epidemiology 1999; 10:17-22).

Emergency Room Visits for the Respiratory Illness in the Elderly Linked to Air Pollution

Consistent with reports of aggravated symptoms in those with chronic respiratory conditions, a study in **Montreal, Canada** found strong associations between air pollution and emergency room visits for patients over 64 years of age during 1993, when more data were available. Positive associations were reported for ozone, PM_{10}, $PM_{2.5}$, and sulfate, at air pollution levels well below the U.S. air quality standards. The elderly are especially susceptible to the effects of air pollution.

The NMMAPS study, discussed above, reported strong and consistent associations between particulate air pollution and hospital admissions among the elderly for cardiovascular disease, pneumonia, and chronic obstructive pulmonary disease.

Delfino, R.J., Murphy-Moulton, A.M., Burnett, R.T., Brook, J.R., and Becklake, M.R. Effects of Air Pollution on Emergency Room Vi for Respiratory Illnesses in Montreal, Quebec. Am J Respir Crit Care Med 1997; 155:568-576.

INFANT MORTALITY AND EFFECTS ON CHILDREN

Doctor Visits Climb In Relation to Air Pollution

In **Paris, France**, doctors still make house calls, and public records on the reason for the visits are available through the French national health insurance program. This enabled investigators to examine a significant but understudied health endpoint, doctor visits, that affects a much larger number of patients than those admitted to hospitals or treated in emergency departments of hospitals. The statistical model of daily air pollution effects used in this study controlled for season, pollen counts, influenza epidemics and weather. Medina et al. report that house calls for asthma for children 0-14 years old showed the strongest association with air pollution.

Medina, S., Le Tertre, A., Quenel, P., Le Moullec, Y., Lameloise, P., Guzzo, J.C., Festy, B., Ferry, R., and Dab, W. Air Pollution and Doctors' House Calls: Results from the ERPURS System for Monitoring the Effects of Air Pollution on Public Health in Greater Paris France, 1991-1995. Environmental Research 75, 73-84, 1997.

Air Pollution May Contribute to Infant Mortality

A small but growing body of literature suggests that air pollution may contribute to infant mortality. British scientists Bobak and Leon analyzed infant mortality and several measures of long-term exposure to air pollutants in highly polluted regions of the **Czech Republic**. They found a consistent, positive association between PM_{10} levels and post neonatal infant mortality from respiratory causes, after controlling for socioeconomic factors and other pollutants.

Dr. Dana Loomis, of the University of North Carolina, and co-workers found that air pollution is associated with acute increases in infant mortality in **Mexico City** after controlling for temperature and other factors. Increases in fine particles, ozone and nitrogen dioxide resulted in an increased number of infant deaths 3 to 5 days later. The effect of particles was the most consistent and the least sensitive to the presence of other pollutants.

A study by EPA scientist Dr. Tracey Woodruff et al., of **86 cities** in the **United States** reported an association between infant mortality and the level of inhalable particles in the first two months of life.

Bobak, M. and Leon, D.A. The Effect of Air Pollution on Infant Mortality Appears Specific for Respiratory Causes in the Postneona Period. Epidemiology 1999;10:666-670.

Loomis, D., Castillejos, M., Gold, D.R., McDonnell, W., and Borja-Aburto, V.H. Air Pollution and Infant Mortality in Mexico City. Epidemiology 1999; 10:118-123.

Woodruff, T.J., Grillo, J., and Schoendorf, K.C. The Relationship Between Selected Causes of Postneonatal Infant Mortality and Particulate Air Pollution in the United States. Environ Health Perspect 1997; 105:607-612.

Air Pollution In Highly Polluted Regions May Cause Low Birth Weight Infants

Low birth weight is the most important predictor for neonatal mortality in developed and developing countries, and is a significant determinant of infant health and survival. A large study in **Beijing, China** looked at maternal exposure to air pollution during pregnancy and subsequent birth weight of infants. Coal stoves used for heating and cooking are a major source of indoor and outdoor air pollution in the study region. Xiaobin Wang of the Boston University School of Medicine and colleagues found a significant exposure-response relationship between maternal exposure to sulfur dioxide and total suspended particles during the third trimester of pregnancy and low birth weight.

Wang, X., Ding, H., Ryan, L., and Xu, X. Association Between Air Pollution and Low Birth Weight: A Community-Based Study. En Health Perspect (1997); 105:514-520.

ASTHMA EXACERBATION

Children's Emergency Room Visits for Asthma Increase on High Air Pollution Days

"*Asthma is the most common chronic illness in children and the cause of most school absences*," state Norris et al., in their study of children's emergency department visits for asthma. University of Washington investigators found significant associations between pediatric hospital visits for asthma and increased daily concentrations of PM and carbon monoxide in **Seattle**. Significantly, exacerbation of asthma was evident even when daily $PM_{2.5}$ concentrations were substantially below the level of the newly adopted National Ambient Air Quality Standard of 15 ug/m^3 annually.

In perhaps the largest study of pediatric asthma visits to date, Dr. Paige Tolbert, of the Rollins School of Public Health at Emory University, and co-investigators, obtained data on emergency department visits for three summers from seven large **Atlanta** area hospitals. The study included information on a variety of pollutants including spatial resolution of ozone data, a broad range of exposure levels, and a balanced distribution of socioeconomic status in the study population.

Increases in both ozone and particulate matter were found to heighten the risk of pediatric emergency room visits for acute asthma. According to the authors, "*the study suggests continuing health risks at pollution levels that commonly occur in many U.S. cities*," and
"*supports accumulating evidence regarding the relation of air pollution to childhood asthma exacerbation*."

Norris, G., YoungPong, S.N., Koenig, J.Q., Larson, T.V., Sheppard, L., and Stout, J.W. An Association Between Fine Particles and A Emergency Department Visits for Children in Seattle. Environ Health Perspect 107:489-493 (1999).

Tolbert, P.E., Mulholland, J.A., MacIntosh, D.D., Xu, F., Daniels, D., Devine, O.J., Carlin, B.P., Klein, M., Dorley, J., Butler, A.J., Nordenberg, D.F., Frumkin, H., Ryan, P.B., and White, M.C. Air Quality and Pediatric Emergency Room Visits for Asthma in Atlanta Georgia. Am J Epidemiol 2000;151:798-810.

Children with Asthma are More Susceptible to Respiratory Effects

Increased particle concentrations have been associated with acute reductions in lung function and increased symptom reporting in children, including children with asthma. Dr. Sverre Vedal, Professor of Medicine at the University of British Columbia, and co-workers followed a group of 2,200 elementary school children in a pulp mill community on **Vancouver Island,** in Canada. Concentrations of potentially important copollutants such as sulfur dioxide, ozone, and acid aerosol were very low in the study community.

Vedal et al. found that children experience declines in peak expiratory flow, a measure of respiratory function, and increased symptoms such as cough, phlegm production, and sore throat, after increases in relatively low 24-hour PM_{10} concentrations. Children with asthma were found to be more susceptible to these effects than other children.

Vedal, S., Petkau, J., White, R., and Blair, J. Acute Effects of Ambient Inhalable Particles in Asthmatic and Nonasthmatic Children. A Respir Crit Care Med 1998, Vol. 157, No. 4, 1034-1043.

Particulate Pollution Worsens Bronchitis in Asthmatic Children

A University of Southern California School of Medicine study of more than 3,600 fourth, seventh and tenth grade children relied on parent questionnaires to identify children with pre-existing asthma or wheeze, and to assess their bronchitic symptoms. The students lived in **12 communities in Southern California** with a broad range of air pollution levels: **Alpine; Atascadero; Lake Elsnore; Lake Gregory; Lancaster; Lompoc; Long Beach; Mira Loma; Riverside; San Dimas; Santa Maria; and Upland, California**. Children with asthma were much more likely than other children to experience bronchitis and phlegm in relation to PM_{10} exposures.

McConnell, R., Berhane, K., Gilliland, F., London, S.J., Vora, H., Avol, E., Gauderman, W.J., Margolis, H.G., Lurmann, F., Thomas, D.C and Peters, J.M. Air Pollution and Bronchitic Symptoms in Southern California Children with Asthma. Environ Health Perspect 107:7 760 (1999).

Peters, J.M., Evol, E., Navidi, W., London, S.J., Gauderman, W.J., Lurmann, F., Linn, W.S., Margolis, H., Rappaport, E., Hong, J. Jr., a Thomas, D.C. A Study of Twelve Southern California Communities with Differing Levels and Types of Air Pollution; I. Prevalence o Respiratory Morbidity. Am J Respir Crit Care Med 1999; 159L760-767.

Etzel, Ruth A. Research Highlights: Air Pollution and Bronchitic Symptoms in Southern California Children With Asthma. Environ H Perspect Vol. 107, No. 9, September 1999.